

**WHAT IS CLAIMED IS:**

1                   1.     A method for identifying a ligand for a receptor comprising the  
2 steps of:

3                         a) providing a substrate comprising an adsorbent wherein the  
4 receptor is bound to the adsorbent;

5                         b) exposing the bound receptor to a sample containing the ligand  
6 under conditions to allow binding between the receptor and the ligand; and

7                         c) detecting bound ligand by desorption spectrometry.

1                   2.     A method of detecting a genetic package containing a  
2 polynucleotide that encodes a polypeptide agent that specifically binds to a target  
3 adsorbent, the method comprising the steps of:

4                         a) providing a substrate comprising a target adsorbent;

5                         b) providing a display library that comprises a plurality of different  
6 genetic packages, each different genetic package comprising a polynucleotide that  
7 comprises a nucleotide sequence that encodes a polypeptide agent, and each different  
8 genetic package having a surface on which the encoded polypeptide agent is displayed;

9                         c) exposing the substrate to the display library under elution  
10 conditions to allow specific binding between a polypeptide agent and the target adsorbent,  
11 whereby a genetic package comprising the polypeptide agent is retained on the substrate;  
12 and

13                         d) detecting a genetic package retained on the substrate by  
14 desorption spectrometry.

1                   3.     The method of claim 2 wherein the display library is a phage  
2 display library.

1                   4.     The method of claim 2 wherein the step of providing the substrate  
2 comprising the target adsorbent comprises the steps of:

3                         i) providing a substrate comprising an adsorbent, wherein  
4 the adsorbent retains a target analyte under an elution condition; and

5 ii) exposing the adsorbent to the target analyte under the  
6 elution condition to allow retention of the target analyte by the adsorbent, whereby the  
7 target analyte becomes the target adsorbent.

1 5. The method of claim 2 further comprising the step of (e)  
2 sequencing the nucleotide sequence that encodes the polypeptide agent.

1 6. The method of claim 2 further comprising the step of (e) isolating  
2 the retained genetic package.

1 7. The method of claim 2 further comprising the step of (e) producing  
2 the polypeptide agent.

1 8. The method of claim 2 wherein the substrate comprises (1) an  
2 adsorbent that binds an anchoring polypeptide and (2) at least one target genetic package  
3 having a surface displaying the anchoring polypeptide and a target adsorbent polypeptide,  
4 the target genetic package comprising a polynucleotide that comprises a nucleotide  
5 sequence that encodes the target adsorbent, wherein the target genetic package is bound  
6 to the adsorbent through the anchoring polypeptide.

1 9. The method of claim 2 wherein the substrate comprises a cell or  
2 cell membrane.

1 10. The method of claim 2 wherein the target adsorbent comprises a  
2 polypeptide that is differentially expressed between cells of different phenotypes.

1 11. The method of claim 3 wherein the phage is M13.

1 12. The method of claim 4 wherein the target analyte is a target  
2 polypeptide and the step of ii) exposing the adsorbent comprises the step of producing the  
3 target polypeptide *in situ* on the adsorbent by *in vitro* translation of a polynucleotide  
4 encoding the target polypeptide.

1                   13.     The method of claim 5 wherein the step of sequencing comprises  
2     amplifying the polynucleotide sequence *in situ* on the substrate.

1                   14.     The method of claim 7 wherein the step of producing comprises  
2     reproducing the retained genetic package that displays the polypeptide agent.

1                   15.     The method of claim 7 comprising expressing the polypeptide agent  
2     from an expression vector that comprises an expression control sequence operatively  
3     linked to the nucleotide sequence encoding the polypeptide agent.

1                   16.     The method of claim 7 further comprising the step of producing a  
2     substrate comprising an adsorbent that comprises the polypeptide agent.

1                   17.     The method of claim 8 wherein the at least one target genetic  
2     package is selected from a target display library screened for genetic packages that bind  
3     at least one primary target analyte and wherein the adsorbent comprises the primary  
4     target analyte.

1                   18.     The method of claim 11 wherein the polypeptide agent is a single  
2     chain antibody.

1                   19.     The method of claim 12 wherein the target polypeptide is produced  
2     *in situ* by *in vitro* translation of a polynucleotide encoding the target polypeptide.

1                   20.     The method of claim 14 wherein the step of reproducing is carried  
2     out *in situ* on the substrate.

1                   21.     The method of claim 19 wherein the polynucleotide encoding the  
2     target polypeptide is produced *in situ* by *in vitro* transcription.

3                   22.     A substrate for desorption spectrometry comprising an adsorbent  
4     that binds an anchoring polypeptide displayed on a surface of a genetic package, wherein  
5     the surface of the genetic package further displays a target polypeptide and wherein the

6 genetic package comprises a polynucleotide comprising a nucleotide sequence that  
7 encodes the target polypeptide.

1 23. The substrate of claim 22 wherein the genetic package is an M13  
2 phage.

1 24. The substrate of claim 22 wherein the anchoring polypeptide is a  
2 fusion polypeptide with gene III protein and the target polypeptide is a fusion polypeptide  
3 with gene VIII protein.

1 25. A substrate comprising an adsorbent that comprises a polypeptide  
2 agent that specifically binds to a target analyte, the polypeptide agent identified by the  
3 method of claim 33.

1 26. The substrate of claim 25 wherein the polypeptide agent is a single  
2 chain antibody.

1 27. A method for detecting translation of a polynucleotide comprising  
2 the steps of:

3 a) providing a substrate comprising an adsorbent for use in  
4 desorption spectrometry;

5 b) contacting the substrate with the polynucleotide encoding a  
6 polypeptide and with agents for *in vitro* translation of the polynucleotide, whereby the  
7 polypeptide is produced;

8 c) exposing the substrate to an eluant to allow retention of the  
9 polypeptide by the adsorbent; and

10 d) detecting retained polypeptide by desorption spectrometry;

11 whereby detection of the polypeptide provides detection of  
12 translation of the polynucleotide.

1 28. A method comprising the steps of:

2 a) exposing a first sample to a primary adsorbent and to an eluant  
3 to allow retention of a first analyte by the adsorbent, and detecting the adsorbed analyte

4 by desorption spectrometry, whereby the retained first analyte becomes a secondary  
5 adsorbent;

6 b) exposing a second sample to the secondary adsorbent and to an  
7 eluant to allow retention of a second analyte by the secondary adsorbent, and detecting  
8 the adsorbed second analyte by desorption spectrometry, whereby the retained second  
9 analyte becomes a tertiary adsorbent.

1 29. The method of claim 28 further comprising repeating step (b) at  
2 least once for a subsequent sample or samples.

1 30. A screening method for determining whether an agent modulates  
2 binding between a target analyte and an adsorbent comprising the steps of:

3 a) providing a substrate comprising an adsorbent to which the target  
4 analyte binds under an elution condition;

5 b) exposing the substrate to the target analyte and to the agent  
6 under the elution condition to allow binding between the target analyte and the adsorbent;

7 c) detecting an amount of binding between the target analyte and  
8 the adsorbent by desorption spectrometry; and

9 d) determining whether the measured amount is different than a  
10 control amount of binding when the substrate is exposed to the target analyte under the  
11 elution condition without the agent;  
12 whereby a difference between the measured amount and the control  
13 amount indicates that the agent modulates binding.

1 31. The method of claim 30 wherein the adsorbent comprises a ligand  
2 that specifically binds the target analyte.

1 32. The method of claim 30 wherein the adsorbent comprises a genetic  
2 package having a surface that displays a polypeptide ligand that specifically binds the  
3 target analyte.

1                    33.    The method of claim 30 for screening a combinatorial library of  
2 agents comprising exposing each of a plurality of agents in the library to each of a  
3 plurality of the adsorbents.

1                    34.    The method of claim 31 wherein the ligand is an enzyme and the  
2 target analyte is a substrate of, or an inhibitor for, the enzyme, or vice-versa.

1                    35.    The method of claim 31 wherein the ligand is a hormone and the  
2 target analyte is a cell surface receptor or an intracellular receptor of the hormone, or  
3 vice-versa.